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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Collin J. Weber, et al.  
Serial No. : 09/049,865 Examiner: Not Yet Known  
Filing Date : March 27, 1998 Group Art Unit: 1643  
For : METHOD OF INHIBITING IMMUNE SYSTEM  
DESTRUCTION OF TRANSPLANTED VIABLE CELLS

1185 Avenue of the Americas  
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July 27, 1998

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

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INFORMATION DISCLOSURE STATEMENT

In accordance with the duty to disclose under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following references:

1. Goosen et al., (1987) Microencapsulation of Living Tissue and Cells, U.S. Patent No. 4,673,566, issued Jun. 16, 1987 (Exhibit 1).
2. Linsley, P.S., (1992) Ligand For CD28 Receptor On B Cells And Methods. WO 92/00092, issued Jan. 9, 1992 (Exhibit 2).
3. Linsley, P.S. (1992) CTL4A Receptor, Fusion Proteins Containing It And Uses Thereof. WO 93/00431, issued Jan. 7, 1993 (Exhibit 3).
4. Linsley, P.S. (1994) Methods For Regulating The Immune Response Using CTLA4-Binding Molecules And IL4-Binding Molecules. EPO 0 613 944 A2, date of publication Sept. 7, 1994 (Exhibit 4).

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5. Linsley, P.S. et al., (1995) Chimeric CTLA4 Receptor And Methods For Its Use, U.S. Patent No. 5,434,131, issued Jul. 18, 1995 (Exhibit 5).
6. Tsang et al., (1987) Encapsulation of Materials, U.S. Patent No. 4,663,286, issued May 5, 1987 (Exhibit 6).
7. Aomatsu, Y. et al., (1994) "Indefinite Graft Survival of Discordant Islet Xenografts in the NOD Mouse With Agarose Microencapsulation and 15-Deoxyspergualin", Transplantation Proc., 26(2):805-06 (Exhibit 7).
8. Aomatsu, Y. et al., (1995) "Significance of Low Doses of 15-Deoxyspergualin in Agarose-Microencapsulated Discordant Islet Xenotransplantation", Islet Xenotransplantation, 292-93 (Exhibit 8).
9. Auchincloss, H., (1988) "Xenogeneic Transplantation", Transplantation, 46(1):1-20 (Exhibit 9).
10. Blazar, B.R., et al. (1993) "In Vivo Infusion of Soluble CTLA4-Ig Reduces Lethal Graft-Versus-Host Disease (GVHD) Induced Across the Major Histocompatibility Complex (MHC) Barrier in Mice", Blood, 82(10):456a.1809 (Exhibit 10).
11. de Vos, P. et al., (1994) "Possible Relationship Between Fibrotic Overgrowth of Alginate-Polysine-Alginate Microencapsulated Pancreatic Islets and the Microcapsule Integrity. Transplantation Proc., 26(2):782-83 (Exhibit 11).
12. Forty, J. et al., (1992) "Hyperacute Rejection of Rabbit Hearts by Human Blood is Mediated by the Alternative Pathway of Complement", Transplantation Proc., 24(2):488-89 (Exhibit 12).

13. Iwata, H. et al., (1992) "Marked Prolongation of Islet Xenograft Survival (Hamster to Mouse) by Microencapsulation and Administration of 15-Deoxyspergualin", Transplantation Proc., 24(4):1517-18 (Exhibit 13).
14. Krych, M. et al., (1992) "Complement receptors", Current Opinion in Immunology, 4(1):8-13 (Exhibit 14).
15. Lacy, P., (1993) "Status of islet cell transplantation", Diabetes Rev., 1(1):76-92 (Exhibit 15).
16. Lafferty, K. et al., (1988) "Circumventing rejection of islet grafts: an overview", In: Van Schilfgaarde, R., and Hardy, M. (eds.), Transplantation of the Endocrine Pancreas in Diabetes Mellitus. Elsevier Science Publishers B.V. (Biomedical Division), 279-91 (Exhibit 16).
17. Lanza, R. et al., (1995) "A Simple Method For Transplanting Discordant Islets Into Rats Using Alginate Gel Spheres", Transplantation, 59(10):1485-87 (Exhibit 17).
18. Lenschow, D. et al., (1992) "Long-Term Survival of Xenogeneic Pancreatic Islet Grafts Induced by CTLA4Ig", Science, 257(5071):789-92 (Exhibit 18).
19. Mazaheri, R. et al., (1991) "Transplantation of Encapsulated Allogenic Islets Into Diabetic BB/W Rats: Effects of Immunosuppression", Transplantation, 51(4):750-54 (Exhibit 19).
20. Pearson, T.C. et al., (1994) "Transplantation Tolerance Induced by CTLA4-Ig", Transplantation, 57(12):1701-06 (Exhibit 20).

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21. Platt, J. et al., (1991) "The Barrier to Xenotransplantation", Transplantation, 52(6):937-47 (**Exhibit 21**).
22. Platt, J. et al., (1991) "The Role of Natural Antibodies in the Activation of Xenogeneic Endothelial Cells", Transplantation, 52(6):1037-43 (**Exhibit 22**).
23. Rabinovitch, A. et al., (1990) "Cytotoxic Effects of Cytokines on Human Pancreatic Islet Cells in Monolayer Culture", J. Clinical Endocrinology & Metabolism, 71(1):152-56 (**Exhibit 23**).
24. Ricker, A. et al., (1986) "Hyperimmune Response to Microencapsulated Xenogeneic Tissue in Non Obese Diabetic Mice", In: The Immunology of Diabetes Mellitus, Jaworski, M. (ed.), Elsevier, Amsterdam, 193-200 (**Exhibit 24**).
25. Ricordi, C. et al., (1987) "Low-temperature culture of human islets or in vivo treatment with L3T4 antibody produces a marked prolongation of islet human-to-mouse xenograft survival", Proc. Natl. Acad. Sci. USA, 84:8080-84 (**Exhibit 25**).
26. Soon-shiong, P. et al., (1992) "Successful Reversal of Spontaneous Diabetes in Dogs by Intraperitoneal Microencapsulated Islets", Transplantation, 54(5):769-74 (**Exhibit 26**).
27. Weber, C. et al., (1989) "Microencapsulated Dog and Rat Islet Xenografts Into Streptozotocin-Diabetic and NOD Mice", Hormone and Metabolic Res., Supplement series 25:219-26 (**Exhibit 27**).
28. Weber, C. et al., (1990) "The Role of CD4+ Helper T Cells in

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the Destruction of Microencapsulated Islet Xenografts in NOD Mice", Transplantation, 49(2):396-404 (**Exhibit 28**).

29. Weber, C. et al., (1990) "Prolonged Functional Survival of Rat-to-NOD Mouse Islet Xenografts by Ultraviolet-B(UV-B) Irradiation Plus Microencapsulation of Donor Islets" Transplantation Proc., 23(1):764-66 (**Exhibit 29**).
30. Weber, C. et al., (1993) "Humoral Reaction to Microencapsulated Rat, Canine, and Porcine Islet Xenografts in Spontaneously Diabetic NOD Mice", Transplantation Proc., 25(1):462-63 (**Exhibit 30**).
31. Weber, C. et al., (1994) "NOD Mouse Peritoneal Cellular Response to Poly-L-Lysine-Alginate Microencapsulated Rat Islets", Transplantation Proc., 26(3):1116-19 (**Exhibit 31**).

The subject application is a continuation-in-part application of PCT International Application No. PCT/US96/15577, filed September 27, 1996, claiming priority of U.S. Provisional Application No. 60/004,375, filed September 27, 1995.

Each of the above-listed references is listed again on the accompanying PTO Form 1449 (**Exhibit A**), and copies of references 1-31 are attached hereto as **Exhibits 1-31**, respectively.

References 17, 18, and 26 were cited in the International Search Report issued in connection with PCT International Application PCT/US96/15577. A copy of the International Search Report is attached hereto as **Exhibit B**.

Applicants maintain that the subject invention is novel and unobvious over the teachings disclosed in the above-referenced publications. Accordingly, applicants maintain that none of the above-listed publications discloses or suggests the invention

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claimed in the subject application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

Under 37 C.F.R. §1.97(b), no fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

Albert Wai-Kit Chan

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:  
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